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Variation in *Salmonella typhi* Infection Among Local Populations in Southern Benue, Nigeria

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Abstract

Background: Typhoid fever caused by *Salmonella typhi* is endemic in many developing countries.
Objective: This study aimed to investigate the prevalence of *S. typhi* in patients attending secondary health centers within the 9 local government areas (LGAs) of Benue.
Materials and Methods: A total of 1022 stool samples, from 583 (57.0%) males and 439 (43.0%) females were collected from patients diagnosed using Widal reaction between August 2016 and July 2017. Selenite broth, Salmonella-Shigella agar, Xylose Lysine Deoxycholate agar and Bismuth Sulfite agar were used for isolation. *S. typhi* was identified using cultural and biochemical characteristics. Univariate analysis and multivariate logistic regression were performed to analyze the collated data.
Results: A high prevalence of *S. typhi* (43.7%, n = 447) and significant differences were observed ($P < 0.05$) in the study site, age, sex and month of sampling. Oju LGA accounted for the highest rate, 64.2% (n = 123). *S. typhi* infection was highest in patients aged ≤10 years (52.7%, n = 243). Males had a significantly higher isolation frequency of 46.8% (adjusted odds ratio [AOR] = 1.321, CI = 1.027–1.700) than females (39.6%). Isolation rates were higher between January (50.0%, n = 31) and May (61.8%, n = 76). Some Widal positive samples were negative for *S. typhi* upon culturing.
Conclusion: These findings suggest the existence of a significant public health hazard which can negatively affect the livelihood of rural dwellers. There is a need for a review of the approach to the diagnoses of typhoid fever in the study area. Increased efforts at sanitation and personal hygiene are advocated.

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Background

Typhoid fever (enteric fever) is caused by *Salmonella typhi* which is solely a human pathogen with no known animal reservoir. *S. typhi* is a gram-negative, motile, rod-shaped and facultative anaerobic bacterium.[1] It is a non-spore forming and non-lactose fermenting bacterium. The bacterium is transmitted mainly through consumption of food and water that has been contaminated by faecal matter.[2] Clean water, good hygiene and sanitation are factors that prevent the spread of typhoid.[1,3,4] The incubation period is usually 1-2 weeks, and the duration of the illness is about 3-4 weeks. Symptoms include poor appetite, headaches, generalized aches and pains, fatigue, weakness, fever as high as 103° to 104°F (39°C to 40°C), lethargy, diarrhoea and rose coloured spot.[5,6]

Salmonella typhi infection begins with colonization of the small intestine, which progresses to the invasion of the gastrointestinal mucosa. The infection then spreads to the liver, spleen, and bone marrow.[1,7] The severity of the infection depends on the initial infective dose, virulence and the host's immune response.[8-10] The greatest burden of disease is experienced by infants, children and adolescents (the World Health Organization [WHO][11] and Crump and Mintz[12]). In view of the above, the WHO recognizes this disease as a major public health problem and recommends immunization with Vi polysaccharide vaccine in high-risk areas.[13]

Typhoid fever is an endemic disease in tropical and sub-tropical climates and has become a major public health problem in developing countries, with an estimated annual incidence of 540 cases per 100 000 people, and an estimated 17 million cases worldwide.[11,14] It is often encountered in tropical countries including Nigeria where it constitutes a serious source of morbidity and mortality.[15,16] This stems from poor hygienic environment and inadequate water supply systems which have become major setbacks in the health systems of Asian, and African countries such as Nigeria.[3,17] In 2004, Crump et al[18] estimated that typhoid fever caused 21.6 million illnesses globally with 216, 510 deaths in the year 2000 alone. Typhoid fever was estimated to have medium incidence in Africa with 10-100 cases per 100 000 persons.[18] However, a recent report has indicated incidence rates higher than 100 cases per 100 000 persons in Burkina Faso, Ghana, Tanzania and Kenya.[19]

A recent study in Nigeria by Akinyemi et al[20] based on blood culture from Widal positive patients between 1993 and 2017, revealed positivity rates of 7% to 18.6% in Lagos, 3.9% to 10.4% in Kano and 0.8% to 2.4% in Abuja. A slight increase in incidence was observed between 2015 and 2017 in Abuja.[20] The incidence of typhoid fever in many parts of Nigeria is not very well known. This has been made difficult by the absence of efficient epidemiological surveillance, coupled with poor or non-existent database of infectious diseases.[20,21] Other contributory factors attributed to the spread of typhoid fever in Nigeria include the absence of adequate human waste processing facilities, abuse of antibiotics, lack of portable drinking water, increase in movement of people and inefficient healthcare delivery systems.[20] Moreover, it is not uncommon to find patients presenting themselves only after patronizing unapproved treatment outlets.[21] The aim of this study, therefore, was to investigate the prevalence of *Salmonella typhi* in patients attending secondary health centers within the 9 local government areas (LGAs) of Benue and the influence of factors such as season, sex and age of patients in the study area.

Materials and Methods

Study Area

The study was conducted in Benue. The area lies within the Guinea savannah region of Central Nigeria (Mid-belt region) and experiences a tropical climate with moderate rainfall estimated to average 1173 mm. The rainy season is experienced from April to October while the dry season runs from November to March.[22] It has a population of about 1 307 647.[23] Benue has 9 LGAs which are Ado, Agatu, Apa, Obi, Ogbadibo, Ohimini, Oju, Okpokwu and Otukpo.

Study Population

The study was hospital-based and was carried out among patients diagnosed with typhoid fever using Widal reaction. The purpose and procedure of the study were explained to the patients (in and out-patients) and demographic information was obtained from each patient through a structured questionnaire.

Sample Collection

A total of 1022 stool samples were collected from patients in Benue State Secondary Health centers within the 9 LGAs of Benue and transported to the Microbiology laboratory of Federal University of Agriculture Makurdi for examination. Samples were collected between August 2016 and July 2017 at various health centers.

Isolation of *Salmonella typhi*

Each sample was first inoculated into Selenite broth base (Oxoid, CM 0395) and incubated for 18-24 hours at 37°C for pre-enrichment. Loopfuls of the broth were then streaked onto Salmonella Shigella agar (Oxoid, CM 0099) and Xylose Lysine Deoxycholate agar (Oxoid, CM 0469). Inoculated plates were incubated at 37°C for 24 hours; suspected colonies were sub-cultured onto Bismuth Sulfite agar (Oxoid, CM 0201) to obtain pure cultures.

Identification of the Isolates

Colonies were identified using their morphological and biochemical characteristics.[24] The shape, color and elevation of the bacterial colony were observed visually. Gram reaction, motility, catalase, indole, oxidase, citrate utilization and Triple sugar iron tests were carried out as described by Ochei and Kolhatkar[25] and Arora and Arora.[26]

Data Analysis

IBM SPSS Statistics version 21.0 (IBM Corp., Armonk, NY, USA) was used to analyze the results obtained. Pearson's chi-square test was used to determine the significance of associations between variables. The strength of the association between infection outcome and controlling variables (age, sex and season) was estimated by crude odds ratio using univariate logistic regression, while multivariate logistic regression model was used to compute adjusted odds ratio with 95% CIs. A P value less than 0.05 was considered statistically significant.

Results

Isolation rate of *S. typhi* in the geographical zones was 43.7% (447/1022) as presented in Table 1. Oju LGA accounted for the highest rate of isolation, 64.2% (79/123) followed by Okpokwu LGA, 55.5% (76/137). Ado LGA had the least rate of isolation, 29.8% (17/57). There was a significant difference in the isolation rate of *S. typhi* in various study sites within Benue ($\chi^2 = 54.293$, $df = 8$, $P < 0.05$).

The prevalence rate of *S. typhi* with respect to age was also determined (Table 2). The age range of ≤10 years has the highest rate of occurrence, 52.7% (128/243), followed by age range 51-60 years with an occurrence rate of 51.4% (19/37). Age group >60 years has the least rate of occurrence, 36.4% (4/11). There was a significant difference in the prevalence rate of *S. typhi* among various age groups ($\chi^2 = 15.316$, $df = 6$, $P < 0.05$). Sex-wise, males had a higher frequency of isolation, 46.8% (273/583), than females, 39.6% (174/439). There was also a significant

Table 1. Isolation Rates of *Salmonella Typhi* in Benue

Study Site	No. Investigated	No. Positive (%)	No. Negative (%)
Ado	57	17 (29.8)	40 (70.2)
Agatu	96	51 (53.1)	45 (46.9)
Apa	83	36 (43.4)	47 (56.6)
Obi	76	30 (39.5)	46 (60.5)
Ogbadibo	176	71 (40.3)	105 (59.7)
Ohimini	60	21(35.0)	39 (65.0)
Oju	123	79 (64.2)	44 (35.8)
Okpokwu	137	76 (55.5)	61 (44.5)
Otukpo	214	66 (30.8)	148 (69.2)

χ^2 = 54.293, *df* = 8, *P* = 0.00 (*P*<0.05).

Table 2. Prevalence Rate of *Salmonella typhi* With Respect to Age and Sex

Demographics	No. Investigated	No. Positive (%)	No. Negative (%)
Age group (y)[a] ≤10	243	128 (52.7)	115 (48.3)
11-20	195	85 (43.6)	110 (56.4)
21-30	292	107 (36.6)	185 (63.4)
31-40	146	64 (43.8)	82 (56.2)
41-50	98	40 (40.8)	58 (59.2)
51-60	37	19 (51.4)	18 (48.6)
>60	11	04 (36.4)	07 (63.6)
Sex[b]			
Male	583	273 (46.8)	310 (53.2)
Female	439	174 (39.6)	265 (60.4)

[a] χ^2 = 15.316, df =6, *P* = 0.02 (*P*<0.05);
[b] χ^2 = 5.263, *P* = 0.02 (*P*<0.05)

Table 3. Seasonal Isolation Rate of *Salmonella typhi* Among Typhoid Fever Patients

Month	No Investigated	No Positive (%)	No Negative (%)
August	42	16 (38.1)	26 (61.9)
September	54	15 (27.8)	39 (72.2)
October	78	19 (24.4)	59 (75.6)
November	123	22 (17.9)	101 (82.1)
December	56	21 (37.5)	35 (62.5)
January	62	31 (50.0)	31 (50.0)
February	84	47 (56.0)	37 (44.0)
March	135	68 (50.4)	67 (49.6)
April	157	92 (58.6)	65 (41.4)
May	123	76 (61.8)	47 (38.2)
June	72	29 (40.3)	43 (59.7)
July	36	11 (30.6)	25 (69.4)
Total	1022	447 (43.7)	575 (56.3)

χ^2 = 94.090, *df* = 11, *P* = 0.00 (*P*<0.05).

difference in the prevalence rate of *S. typhi* in relation to sex (χ^2 = 5.263, *df* = 1, *P* < 0.05).

The seasonal isolation rate of *S. typhi* among patients with suspected typhoid was also determined (Table 3). Table 4 shows the variation in isolation with respect to seasons. High isolation rates were recorded between January, 50.0% (31/62) and May, 61.8% (76/123). November accounted for the least rate of isolation, 17.9% (22/123). There was a significant difference in the prevalence rate of *S. typhi* in relation to the month of sample collection (χ^2 = 94.090, *df* = 11, *P* < 0.05).

The relationship of sex, age and season of sample collection with *S. typhi* infection in patients was also assessed. After adjusting for age, sex and season, males were significantly more prone to get infected (adjusted odds ratio [AOR] = 1.321, CI = 1.027–1.700) than females. Age did not show any significant relationship with *S. typhi* infection (AOR = 0.993, CI = 0.984–1.022). Although the relationship was not significant, *S. typhi* infection was more associated with the rainy season (AOR = 1.223, CI = 0.951–1.572) than the dry season.

Discussion

The findings of this study revealed an isolation rate of 43.7% (447/1022) for *S. typhi* in the study area. This is consistent with those of Mohammed et al[3] and Adabara et al[27] in studies conducted in Nasarawa and Minna in Nasarawa and Niger states, Nigeria respectively. A much higher prevalence was reported by Ifeanyi et al,[16] Kalu et al[28] and Bhatta et al[29] in Abuja and Owerri in Nigeria, and Nepal in Asia, respectively. These findings are in agreement with the position of the WHO[11] that the vast majority of typhoid fever cases occur in Asia, Africa and Latin America where water-borne diseases are highly prevalent. The difference in the isolation rates recorded in various study sites is significant (*P*<0.05). The high isolation rate recorded in Oju LGA could be attributable to the absence of portable water sources as observed in the LGA. The inhabitants of Ado LGA have access to boreholes in the communities which could explain the low rate of isolation of *S. typhi*. The rates of *S. typhi*, including that of the present study, suggest the existence of a significant public health hazard in developing environments.

The difference in the prevalence rate of *S. typhi* within the age groups is significant (*P* < 0.05). This corroborates earlier reports by Adabara et al[27] in Minna, Umeh and Agbulu[30] in Makurdi, Central Nigeria, Nigeria and Pato-Mesola et al[31] in Cebu City, India, though a much higher prevalence was reported. The highest prevalence (52.7%) was observed among patients aged ≤10 years old in the present findings, however, it differs from an earlier study by Akter et al[32] in Dhaka City Bangladesh, where the highest prevalence rate was observed in the age group 21 to 30 years. Individuals older than 60 years of age showed a much lower prevalence rate. It is reasoned that children form the most vulnerable group in environments where inadequate water supply and poor environmental hygiene

Table 4. Association of Risk Factors With *Salmonella typhi* Infection

Risk Factor	No. of Samples	No. Positive (%)	OR (95% CI)	*P* Value	AOR (95% CI)	*P* Value
Sex						
Female		Reference				
Male	439	174 (39.6)	1.341(1.043 – 1.724)	0.022[a]	1.321(1.027 – 1.700)	0.030[a]
Age	1022	447 (43.7)	0.994 (0.985 – 1.002)	0.146	0.993(0.984 – 1.022)	0.12
Season						
Dry season		Reference				
Rainy season	562	258(25.2)	1.217(0.949 – 1.561)	0.122	1.223(0.951 – 1.572)	0.117

OR, crude odds ratio; AOR, adjusted odds ratio.

[a] $P < 0.05$.

are problems. This is because of their level of ignorance which accounts for their quest or desire to satisfy their thirst irrespective of the water source, especially if the water appears to be clean and without color. Their intellectual and mental capability is also not developed enough to maintain required level of hygiene. The high isolation rate recorded in the age group of 51-60 years could be attributable to suppression in their immune system as they grow old.[30] The age group of young adults equally recorded a high isolation rate. The possible causes for enteric fever being common in this age group include the high rate of mobility from one place to another, as well as consumption of poorly prepared or unhygienic food and water in schools and colleges.[12] The implication of this is that the education of the youth which form the workforce of the zone, as well as farming activities which is the main source of economic livelihood, will be affected and its attendant consequences like illiteracy, economic misfortune and hunger will be great. According to the WHO[11] and Crump and Mintz,[12] the burden of typhoid fever is highest in infants, children and young adults. Health education will play an important role in this age group as illiteracy and low educational status is associated with ignorance, poverty and poor personal hygiene.[33,34]

Salmonella typhi isolation rate showed male preponderance over females, suggesting a higher likelihood for men to get infected with S. typhi. This is consistent with earlier findings in different Nigerian cities[16,17,30,35-37] and India.[38] The findings of Abd-Alhafeez and Nafi[6] in Khartoum, Sudan, Cinthujah et al[39] in India and Hayat et al[40] in Pakistan also corroborate this finding. This could be as a result of the cultural orientation of the study area. A male is more likely to report to the hospital, and also likely to contract infection due to engagement in more outdoor activities. It is opined that males usually work outside their homes and may eat hawked foods that are liable to contamination and these habits predispose them to infection.[1,30,33] Additionally, male folks in the study area engage in farming activities away from their abode, which could occasion the consumption of water from contaminated sources.

The majority of the culture-positive stool samples from suspected typhoid patients in this study were obtained in the early raining season. The highest number of *S. typhi* was isolated from February to May. This period marks the tail end of the dry season and the onset of raining season in the study area. The result also reveals a significant variation in the isolation rate of *S. typhi* within the months of January to December ($P < 0.05$). These findings are consistent with those of Adesina et al,[35] Sudeepa et al,[38] Simental and Martinez[41] and Kumar et al.[42] The low rate of *S. typhi* isolation recorded during the dry season could be attributable to the fact that the inhabitants abandon the use of streams, rivers and wells because they get dried up, in pursuance of treated water sold in sachets and bottles by water producing companies. This treated water often contains less contaminants than their hitherto source of water. When the rains set in again, locals return to the use of wells, streams and rivers which could have been contaminated by various unhygienic practices.

Umeh and Agbulu[30] and Okome-Nkoumou et al[43] opined that typhoid fevers are associated with poor environmental and living conditions, especially in economically poor countries. Most communities in the study area lack treated pipe-borne water, toilet facilities and effective waste disposal systems. They get their drinking water from streams, wells and rivers. Unfortunately, they defecate in nearby bushes and indiscriminately dispose domestic wastes in the environment, at sites which, in some cases, are very close to the same streams and rivers that provide water for the communities. The inhabitants in some of these communities equally bathe in the same body of water used for domestic purposes. It is likely that contamination of food materials or drinking water could be as a result of washed-off faecal matter from the environment, debris and littered garbage during early raining season, which runs into streams and wells used as domestic sources of water. These factors could actually increase the risk of person-to-person spread, especially in the communities. Enteric fever cases occurring throughout the year in this study implies a large number of carriers could be present in the society. Provision of potable water and healthcare facilities by authorities at various levels is required in order to put a break to the endemic nature of the infection. To limit the spread of faecal-orally transmitted infections, enlightenment programs on basic rules of hygiene for communities should be encouraged. Disinfection of drinking water either by boiling, chlorination or addition of sodium aluminate (alum) should be encouraged.

Although all patients tested positive for *S. typhi* when Widal test was used, culture method, however, revealed otherwise. This finding further proves that Widal test as a method for diagnosis of typhoid fever in patients may not be as sensitive as the use of culture, which has remained the gold standard test. The use of Widal test could lead to overestimation of typhoid incidence among a population.[19] Unfortunately, most health centers in rural areas within Nigeria lack appropriate materials for diagnosis using culture method, due to its expensive and time-consuming nature. It has, however, been opined that culture method may show negative result especially when the patient has previously used antibiotics.[6] It is thus, imperative for health centers in Nigeria to adopt the use of more sensitive and specific rapid detection methods such as Typhidot-EIA test and dot ELISA for diagnosis of typhoid fever.

Conclusion

The present study shows a high incidence of typhoid (43.5%) in Southern Benue. Although all 1022 patients were diagnosed with typhoid fever using the Widal test, only 447 samples were positive using culture method. Hence, a review of the approach to the diagnosis of typhoid fever in the study area is advocated. Moreover, public enlightenment on good personal and environmental hygiene practices could help reduce the spread of the disease among inhabitants of the area.

Authors' Contributions

Conception and design of the study was done by PA, EUU, CCI and IOO. PA participated in data collection and sampling. PA, GAO and PSA handled drafting and revision of manuscript. Data analysis and interpretation was done by GAO and PA. Final approval of the manuscript was done by all authors.

Ethical Approval

Ethical approval for this study was obtained from the Research Ethical Committee of the Benue State Hospitals Management Board (No. HMB/OFF/215/VOL.I/91).

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

References

1. Harriet U, Nandita D. Mechanisms of Antibiotic resistance in *Salmonella typhi*. Int J Curr Microbiol App Sci. 2014;3(12):461-746.
2. Gonzalez-Escobedo G, Marshall JM, Gunn JS. Chronic and acute infection of the gall bladder by *Salmonella typhi*: Understanding the carrier state. *Nat Rev Microbiol*. 2011;9(1):9-14. doi:10.1038/nrmicro2490.
3. Mohammed SA, Tsaku PA, Nkene IH, Oti VB, Ekeleme IK. Plasmid – mediated resistance in *Salmonella typhi* isolates from Door Handles in Nasarawa State, North-central Nigeria. Asian J Biotech Biores Tech. 2017;1(1):1-12.
4. Santos SA, Andrade Jr. DR, Andrade DR. TNF-production and apoptosis in hepatocytes after *Listeria monocytogenes* and *Salmonella* Typhimurium invasion. Rev Inst Med Trop Sao Paulo. 2011;53(2):107–112.
5. Abdulahi M. Incidence and antimicrobial susceptibility pattern of Salmonella species in children attending some hospitals in Kano metropolis, Kano-State, Nigeria. Bayero Journal of Pure and Applied Sciences. 2010;3(1):202-206. doi: 10.4314/bajopas.v3i1.58787
6. Abd-Alhafeez HA, Nafi M. Comparison of typhidot-eia and widal test in respect to polymerase chain reaction as diagnostic procedures for early diagnosis of typhoid fever. J Biomed Pharm Res. 2014;3(5):18-20.
7. Raffatellu M, Wilson RP, Winter SE, Bäumler AJ. Clinical pathogenesis of typhoid fever. J Infect Dev Ctries. 2008;2(4):260-266.
8. Tsolis RM, Kingsley RA, Townsend SM, Ficht TA, Adams LG, Bäumler AJ. Of mice, calves, and men. Comparison of the mouse typhoid model with other Salmonella infections. Adv Exp Med Biol. 1999;473:261-274.
9. Butler T. Treatment of typhoid fever in the 21st century: promises and shortcomings. Clin Microbiol Infect. 2011;17(7):959-963. doi: 10.1111/j.1469-0691.2011.03552.x.
10. Kaur J, Jain SK. Role of antigens and virulence factors of *Salmonella enterica serovar typhi* in its pathogenesis. Microbiol Res. 2012;167(4):199-210. doi:10.1016/j.micres.2011.08.001
11. World Health Organization. Typhoid vaccine (Initiative for Vaccine Research). Geneva, Switzerland: WHO; 2010.
12. Crump JA, Mintz ED. Global trends in typhoid and paratyphoid fever. Clin Infect Dis. 2010;50(2):241-46. doi: 10.1086/649541.
13. World Health Organization. Typhoid vaccines: WHO position paper. Wkly Epidemiol Rec. 2008; 83(6):49-59.
14. Qamar FN, Azmatullah A, Kazi AM, Khan E, Zaidi AKM. A three-year review of antimicrobial resistance of *Salmonella enterica serovars Typhi* and *Paratyphi A* in Pakistan. J Infect Dev Ctries. 2014;8(9):981-986.
15. Ibekwe AC, Okonko IO, Onumkwo AU, Donbraye E, Babalola ET, Onoja BA. Baseline Salmonella agglutination titres in apparently healthy freshmen in Awka, South Eastern Nigeria. *Sci Res Essay*s. 2008;3(9):225–230.
16. Ifeanyi CIC, Bassey EB, Ikeneche NF, Isu RN, Akpa AC. Prevalence and antimicrobial susceptibility of Salmonella species associated with childhood acute gastroenteritis in Federal Capital Territory Abuja, Nigeria. Br Microbiol Res J. 2013;3(3):431-439.
17. Anita S, Indrayan AK, Guteria BS, Gupta CP. Antimicrobial activity of dye of *Casalpina sappan*. Indian J Microbiol. 2002;42(4):359–360.
18. Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. Bull World Health Organ. 2004;82(5):346-353
19. Marks F, Kalckreuth V, Aaby P, et al. Incidence of invasive salmonella disease in sub-Saharan Africa: a multicentre population-based surveillance study. *Lancet Glob Health*. 2017;5:e310–e23.
20. Akinyemi KO, Oyefolu AOB, Mutiu WB, et al. Typhoid fever: tracking the trend in Nigeria. Am J Trop Med Hyg. 2018; 99(3):1–7. doi:10.4269/ajtmh.18-0045
21. Grema BA, Aliyu I, Michael GC, et al. Typhoid ileal perforation in a semi-urban tertiary health institution in north-eastern Nigeria. S Afr Fam Pract. 2018;60(5):168-173. doi: 10.1080/20786190.2018.1481604.

22. Abah RC. An application of geographic information system in mapping flood risk zones in a North Central City in Nigeria. Afri J Environ Sci Technol. 2013;7(6):365-371.
23. National Population Commission. Federal Republic of Nigeria Official Gazette 2009. 96.
24. Fagbamila IO, Barco L, Mancin M, et al. *Salmonella* serovars and their distribution in Nigerian commercial chicken layer farms. PLoS One. 2017;12(3):e0173097. doi:10.1371/journal.pone.0173097
25. Ochei JO, Kolhatkar A. Medical Laboratory Science and Practice. New York: Tata McGraw-Hill; 2008.
26. Arora DR, Arora B. A Textbook of Microbiology. 3rd ed. New Delhi: CBS publishers; 2001.
27. Adabara NU, Ezugwu BU, Momojimoh A, Madzu A, Hashiimu Z, Damisa D. The prevalence and antibiotic susceptibility pattern of *Salmonella typhi* among patients attending a military hospital in Minna, Niger State, Nigeria. Adv Prev Med. 2012;2012: 875419. doi: 10.1155/2012/875419
28. Kalu IG, Ogbulie TE, Opara FN. Pattern of multidrug resistant *Salmonella enterica* serovar typhi isolates in Nigeria. Afr J Biotechnol. 2008;7(21):3817-3820.
29. Bhatta CP, Bhuyan KC, Maharjan A. Antibiotic sensitivity pattern of *Salmonella* species isolated from blood culture. J Nepal Health Res Counc. 2005;3(2):35-38.
30. Umeh EU, Agbulu C. Distribution pattern of *Salmonella* Typhoidal Serotypes in Benue State, Central Nigeria. The Internet Journal of Epidemiology 2009;8(1):1-7.
31. Pato-Mesola VV, Donaldo MES. Antimicrobial susceptibility of *S. typhi* isolated from Government and Private Hospital in Cebu City. Phil J Microbiol Infect Dis. 1997;26(1):5–8.
32. Akter L, Munir H, Zakaria A. Present status and antibiotic sensitivity pattern of *Salmonella typhi* and *Salmonella paratyphi* in Different Age Group. Hospitalized patients in Dhaka City, Bangladesh. IOSR Journal of Pharmacy and Biological Sciences. 2012;4(3):27-30.
33. Parande MA, Patil CG, Rayate MV, Lukde MU. Epidemiological profile of enteric fever cases admitted in SCSMGH, Solapur. Nat J Community Med. 2011;2(1):91-95.
34. Kanungo S, Dutta S, Sur D. Epidemiology of Typhoid and paratyphoid fever in India. J Infect Developing Countries. 2008;2(6):454-460.
35. Adesina OG, Osuagwu NO, Claire-Lorentz EO, Joseph OE, Bolaji RO. Prevalence and susceptibility of *Salmonella typhi* and *Salmonella paratyphi* in Zaria, Nigeria. Int J Health Res. 2009;2(4):355-360.
36. Akinyemi KO, Iwalokun BA, Oyefolu AOB, Fakorede CO. Occurrence of extended-spectrum and AmpC β-lactamases in multiple drug resistant *Salmonella* isolates from clinical samples in Lagos, Nigeria. Infect Drug Resist. 2016;10:19-25. doi:10.2147/IDR.S123646
37. Okonko IO, Soleye FA, Eyarefe OD, et al. Prevalence of Salmonella typhi among patients in Abeokuta, South-Western, Nigeria. Br J Pharm and Toxicol. 2010;1(1):6-14.
38. Sudeepa KM, Vijaykumar GS, Prakash R, Prashanth HV, Raveesh PM, Nagaraj ER. Comparison of *Salmonella typhi* and Paratyphi A occurrence in a tertiary care hospital. J Clin Diagn Res. 2013;7(12):2724–2726.
39. Cinthujah B, Amudha VP, Sucilathangam G. Comparative Study of Widal and Dot Elisa in the Diagnosis of Typhoid Fever. Int J Sci Res. 2012;3(4):303-304.
40. Hayat AS, Shaikh N, Shah SA. Evaluation of Typhidot (IgM) in early and rapid diagnosis of typhoid fever. Professional Medical Journal. 2011;18(2):259-264.
41. Simental L, Martinez-Urtaza J. Climate pattern governing the presence and permanence of Salmonellae in coaster areas of Bahia de Todos Santos, Mexico. Appl Environ Microbiol. 2008;74(19):5918–5924.
42. Kumar S, Rizvi M, Berry N. Rising prevalence of enteric fever due to multi-drug resistant Salmonella: an epidemiological study. J Med Microbiol 2008;57(10):1247–1250. doi:10.1099/jmm.0.2008/001719-0.
43. Okome-Nkoumu M, Nkana EA, Bekale J, Kombila M. Typhoid and paratyphoid fever in adults in the internal medicine department at Libreville, Gabon. Sante. 2000;10(3):205-209